



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP110090

Project Title:
Inhibiting miR-451 as a novel treatment modality for polycythemia, a pre-leukemic disease

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Huang, Lily J

Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Polycythemia is a pre-leukemic malignancy, associated with the over-production of red blood cells. About 22 in 100,000 people in the U.S. have PV, and many of them will evolve to acute myelogenous leukemia (AML), the most common form of myeloid leukemia in adults. The life expectancy of untreated patients is 18 months. Currently, the main therapy is phlebotomy (bleeding), which entails frequent treatment, sometimes daily. In addition, phlebotomy significantly increases thromboembolic (clotting) complications. Although chemotherapy agents, often used in conjunction, can reduce the number of thrombotic events, they substantially increase the rate of evolution to AML. These issues underscore the need for novel therapeutic strategies. We recently showed that a tiny RNA molecule, called microRNA-451 (miR-451), which is expressed almost exclusively in red blood cells, plays an important role in red blood cell maturation. Mice lacking miR-451 have decreased numbers of red blood cells with no other obvious abnormalities. We thus hypothesize that an inhibitor to miR-451 may be a novel therapeutic agent for polycythemia. In this proposal, we will test if inhibition of miR-451 can diminish the excess red blood cell production in two mouse models of polycythemia. We will also determine the efficacy of miR-451 inhibitors to reduce red blood cell maturation of human hematopoietic stem/progenitors from PV patients. Because miR-451 inhibitors should specifically target red blood cells without affecting other cells involved in thrombosis, this agent may circumvent the need for chemotherapy and prevent the transformation to AML.